

Spinal Muscular Atrophy Newborn Screening Long Term Follow Up

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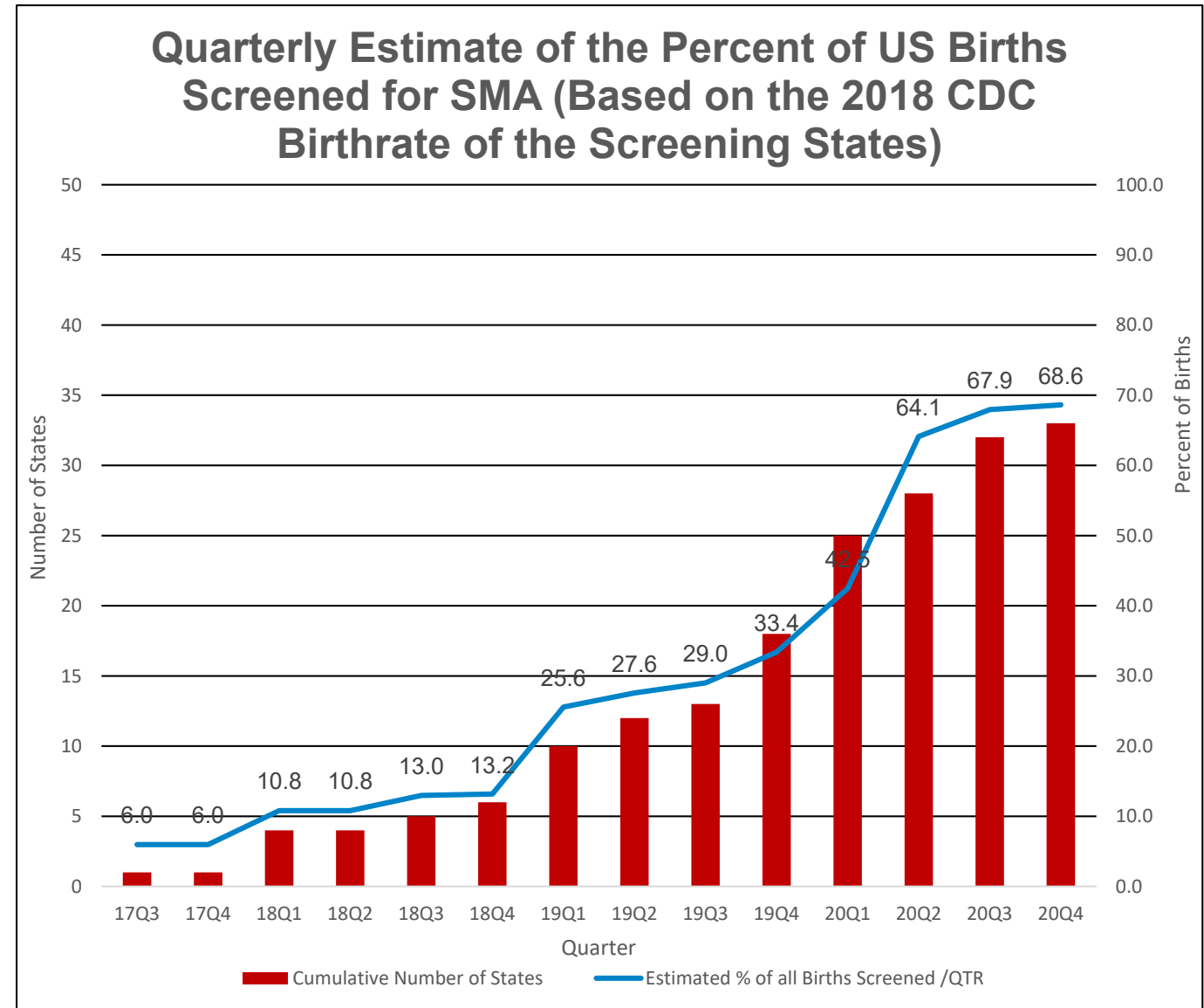
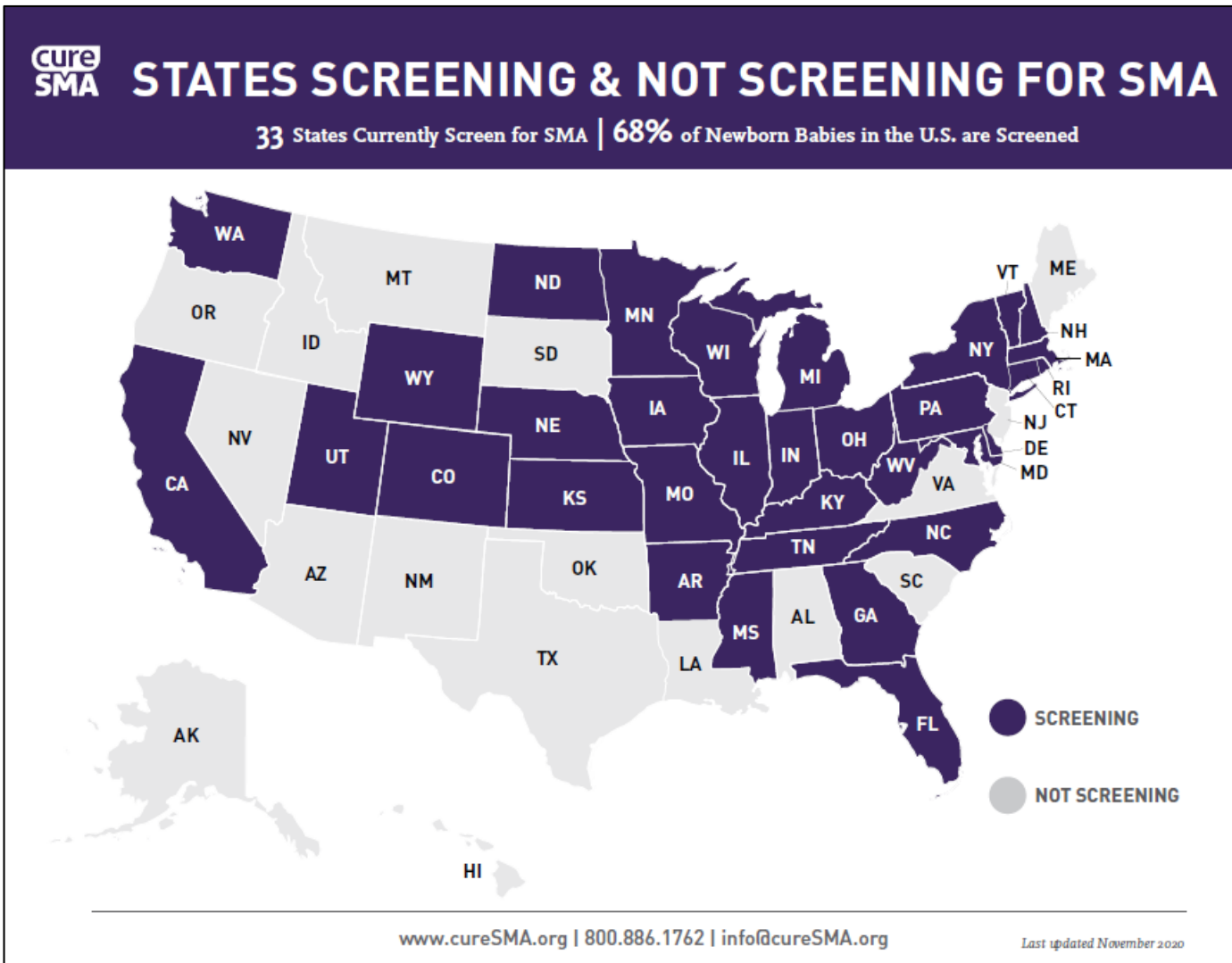


Make today a breakthrough.

About Cure SMA

- Fund and direct comprehensive research that drives breakthroughs in treatment and care.
- Provide vital support services for families living with SMA.
- 36 chapters, volunteer led, face of the organization on the ground.
 - 120,000 families and supporters.
- www.cureSMA.org

SMA Newborn Screening



SMA Newborn Screening Incidence by State

CURE SMA NBS Incidence by State - Prepared 1/22/2021								
Permanent Screening States - 28	Pilot Phase Dates	Permanent Screening Date Start	Reporting Period Start	Reporting Period End	Number Screened	Number Positive	Incidence of 1 in	2018 Birth Rate
Georgia	2/8/2019-3/30/2020	4/1/2020	2/6/2019	12/14/2020	234,795	14	16771	126,172
Illinois		6/29/2020	6/29/2020	11/17/2020	62,992	5	12598	144,815
Indiana	7/1/2018-12/31/2018	1/1/2019	7/1/2018	7/31/2020	169,088	8	21136	81,646
Kansas		2/1/2020	2/1/2020	3/31/2020	6,781	0		36,261
Kentucky		8/13/2019	8/13/2019	8/31/2020	52,622	11	4784	53,922
Maryland		6/17/2019						71,080
Michigan		3/9/2020	1/4/2019	11/17/2020	107,694	11	9790	110,032
Minnesota		3/18/2018	3/18/2018	12/31/2019	120,863	12	10072	67,344
Mississippi		11/1/2019						37,000
Missouri		1/2/2019	1/2/2019	4/17/2020	94,200	10	9420	73,269
Nebraska		11/14/2020						25,488
New Hampshire		12/23/2019						11,995
New York	1/1/2016-9/30/2018	10/1/2018	10/1/2018	11/20/2020	468,935	23	20388	226,238
Pennsylvania		3/1/2019	3/1/2019	10/31/2020	219,950	17	12938	135,673
Rhode Island		7/1/2020						10,506
Tennessee		2/1/2020						80,751
Utah		1/29/2018	1/1/2019	12/31/2020	94,905	6	15818	47,209
Vermont		5/1/2019	5/1/2019	11/24/2020	8,001	0		5,432
Washington		8/7/2020						86,085
West Virginia		11/20/2019						18,248
Wisconsin		10/15/2019	10/15/2019	11/14/2020	66,203	6	11034	64,098
Wyoming		1/20/2020	1/20/2020	10/31/2020	4,438	1	4438	6,562
Infants screened for SMA to Date - Subtotal					2,029,387	146	13900	2,341,537
Pilot Screening States - 5								
Iowa	7/1/2020		7/1/2020	1/22/2020	20,000	0		37,785
North Carolina (opt-in) [Q1 2020]	10/22/2018		10/22/2018	10/1/2020	10,600	1	10600	118,954
North Dakota	7/1/2020		7/1/2020	1/22/2020	6,427	0		10,636
Massachusetts	1/1/2018		1/27/2018	11/17/2020	168,493	10	16849	69,109
Ohio	1/15/2019		1/15/2019	9/30/2020	222,411	16	13901	135,134
Infants screened for SMA to Date - Subtotal					407,931	27	15109	371,618
Infants screened for SMA to Date - Total					2,437,312	173	14,089	

- 25/33 states screening:
 - 2,437,312 Infants Screened (since January 2018)
 - 173 Infants SMA NBS positive
 - 108 families contacted Cure SMA after diagnosis
 - Preliminary estimated incidence 1:14,000









The Evolving Landscape in Spinal Muscular Atrophy

The FDA-approval of **3 SMA Treatments** has revolutionized and dramatically changed the natural history of SMA

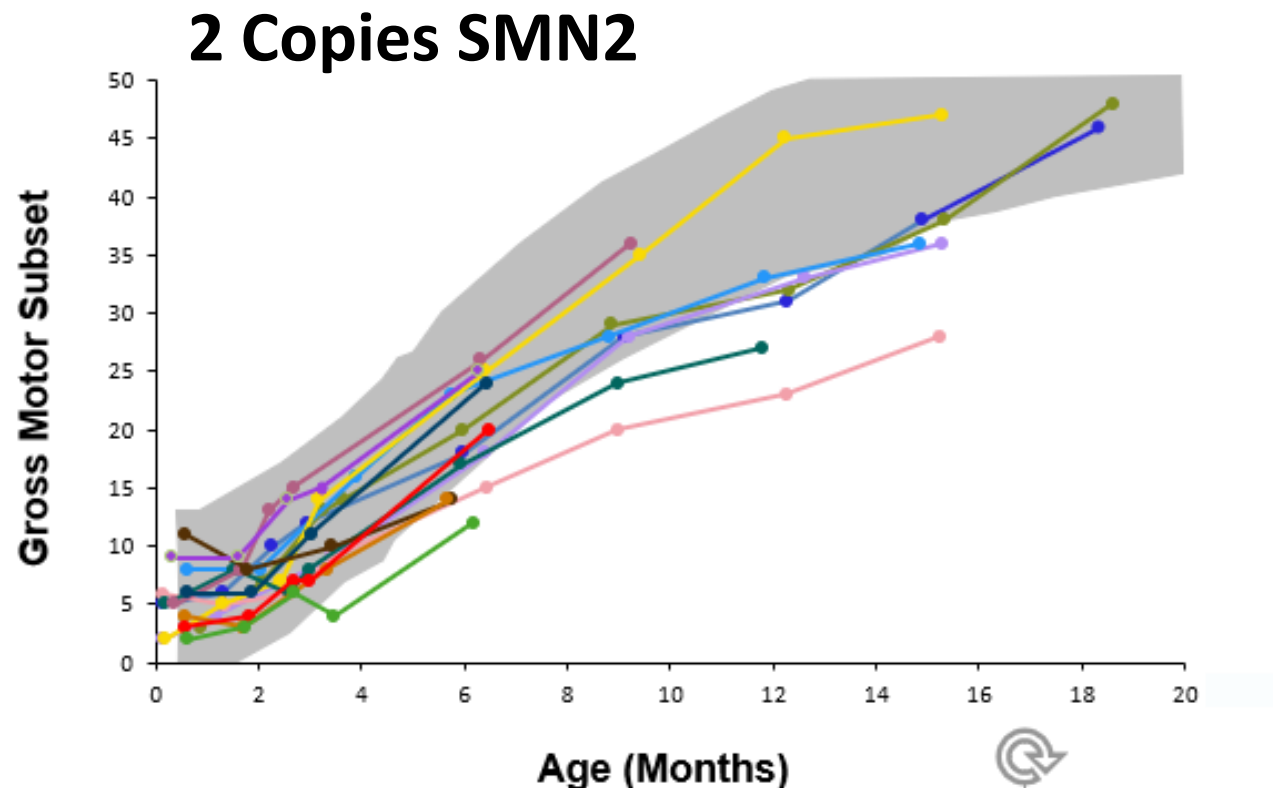
Early identification and treatment are essential to altering long-term outcomes, observed most strikingly in presymptomatic infants

Symptomatic treatment provides improvements **through increases, stabilization, and slowing** disease progression

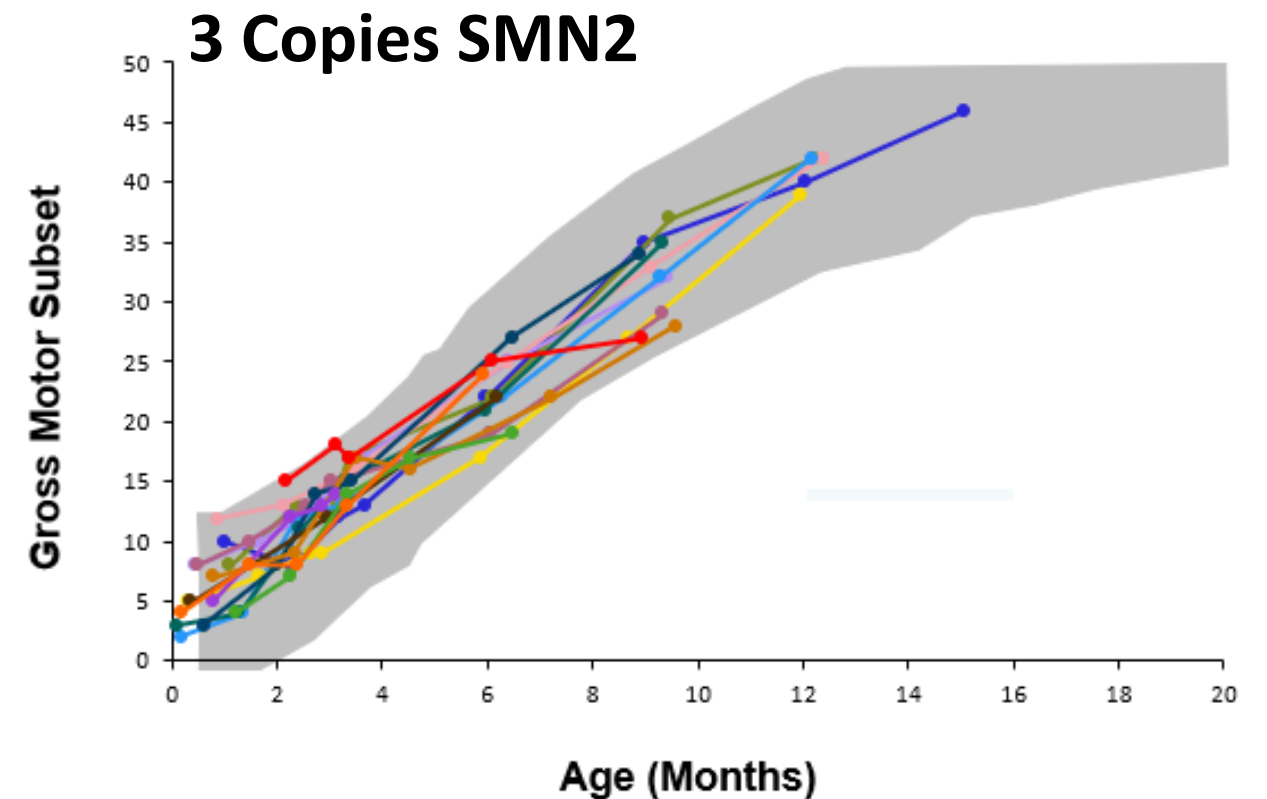
NURTURE (Presymptomatic Nusinersen): WHO Motor Milestone Development

Motor Milestone	<u>3 SMN2 copies</u>	<u>2 SMN2 copies</u>
 Sitting without support	10/10 (100%)	15/15 (100%)
 Standing with assistance	10/10 (100%)	15/15 (100%)
 Hands and knees crawling	10/10 (100%)	14/15 (93%)
 Walking with assistance	10/10 (100%)	14/15 (93%)
 Standing alone	10/10 (100%)	12/15 (80%)
 Walking alone	10/10 (100%)	12/15 (80%)

SPR1NT Trial: Presymptomatic SMA Treatment with Zolgensma: Increases in Mean Bayley-III Gross Motor Score



7 of 14 (50%) age-appropriate gross motor performance
 14 of 14 (100%) age-appropriate fine motor performance



15 of 14 (100%) age-appropriate gross motor performance
 14 of 15 (93%) age-appropriate fine motor performance

Kevin A. Strauss, presentation, Cure SMA Virtual Research and Clinical Care Meeting 2020

SMA Treatments

	Spinraza	Zolgensma	Evrysdi
FDA Approval Year	2016	2019	2020
Type	Antisense oligonucleotide	Single stranded SMN1 DNA via AAV9 vector	Small molecule
Mechanism	SMN2 mRNA splicing modifier	SMN1 functional replacement with SMN1 DNA episome	SMN2 mRNA splicing modifier
Approved age	All	<2 years old	>2 months old
Dose	12 mg/5 ml	1.1×10^{14} vector genomes/Kg body weight	0.2 mg/kg up to 2 yo and 20 kg 0.25 mg/kg >2 yo and <20 kg 5 mg per day > 20 kg Concentration: 0.75 mg/ml
How given	Intrathecal	Intravenous	Enteral (oral or feeding tube)
How often	4 loading doses over 2 months, then every 4 months	One time	Daily
Body distribution	CSF	Blood stream – systemic	Enteral - systemic

Cure SMA Real World Evidence

SMA Newborn Screening Registry

- Family entered survey data about child
- Longitudinal information
- Linked to Clinical Data Registry

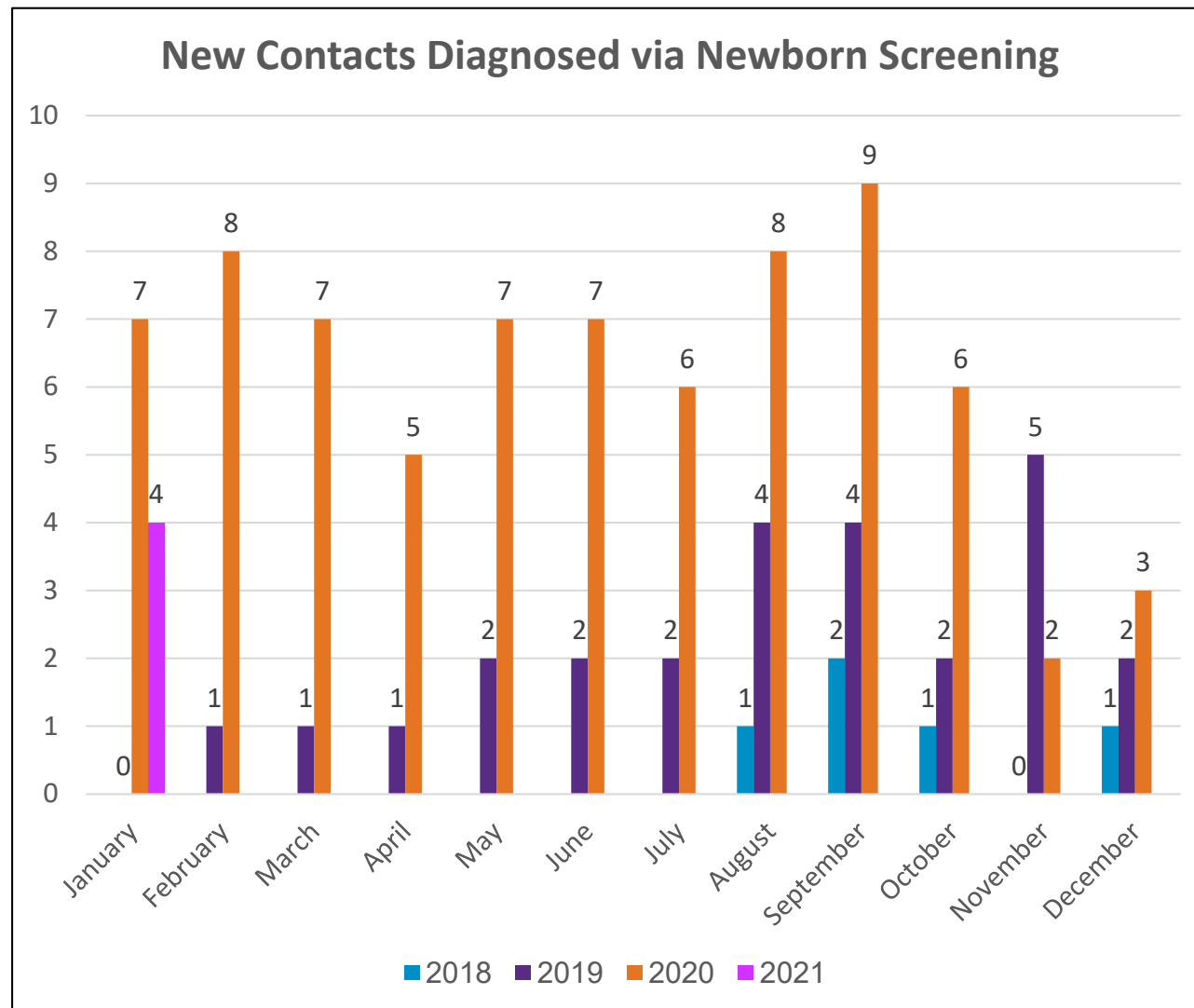
Cure SMA Membership Database

- Family and patient reported data and outcomes
- Annual Community Survey
- Assist with recruitment for clinical trials and surveys
- Data for regulatory officials, payers, industry partners, and healthcare providers

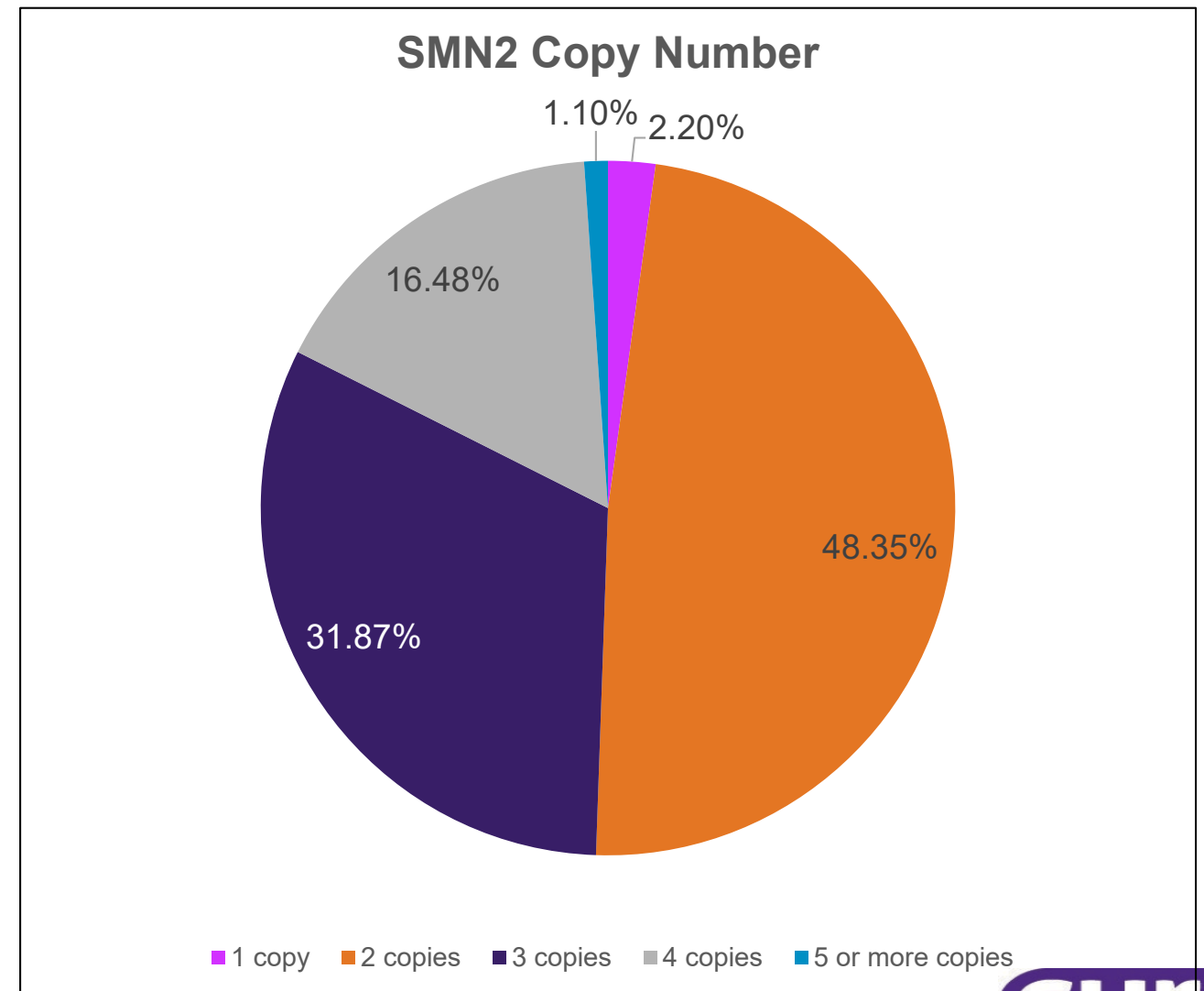
SMA Clinical Data Registry (CDR)

- Clinician entered data
- Data transferred from electronic medical record electronically to SMA CDR

Cure SMA Membership Database:



Total=110



Total=91

Cure SMA NBS Portal Survey

- Survey for families with NBS identified child with SMA
- Parent provides consent
 - Parent or healthcare provider can complete survey
 - Separate portals for families and healthcare providers
- www.curesma.org/NBSR

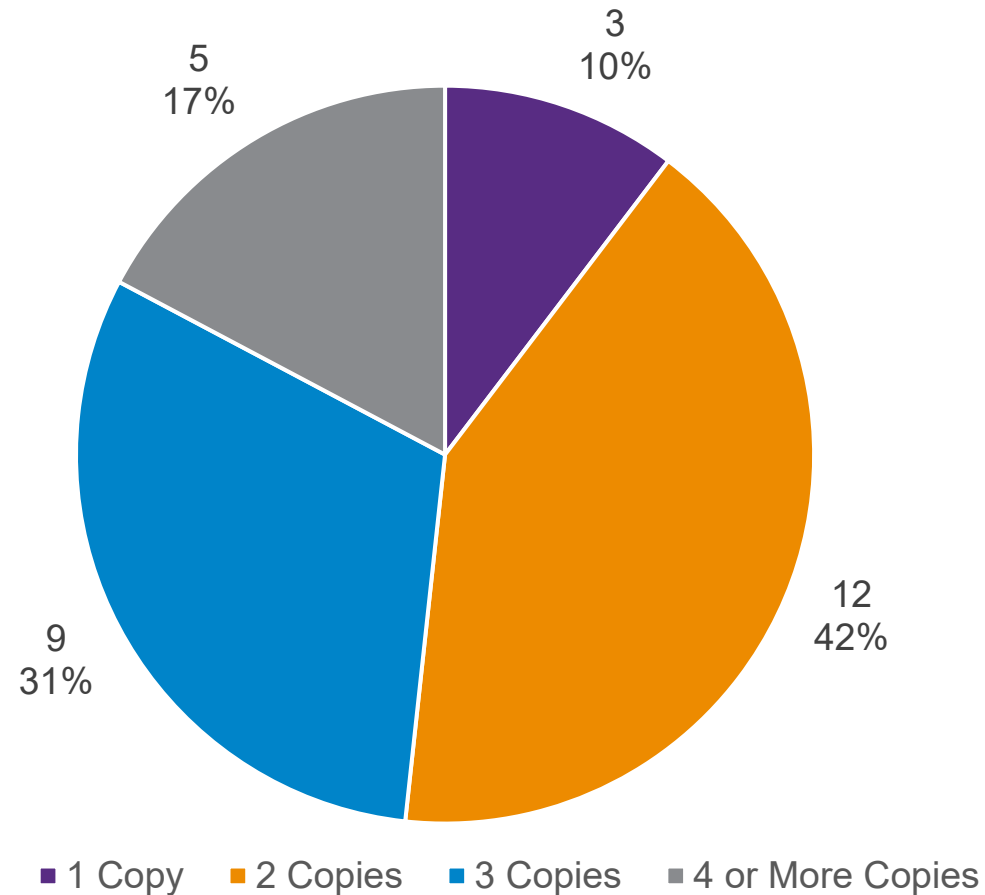


Support provided by the **Cure SMA Newborn Screening Coalition**.
Members include Cure SMA, Novartis Gene Therapies and Genentech,
A Member of the Roche Group



Cure SMA Newborn Screening Registry:

SMN2 Copy Number



Treatment Status by SMN2 Copy Number



N=29

Cure SMA Newborn Screening Registry: Median Age at Diagnosis and Treatment by SMN2 Copy Number

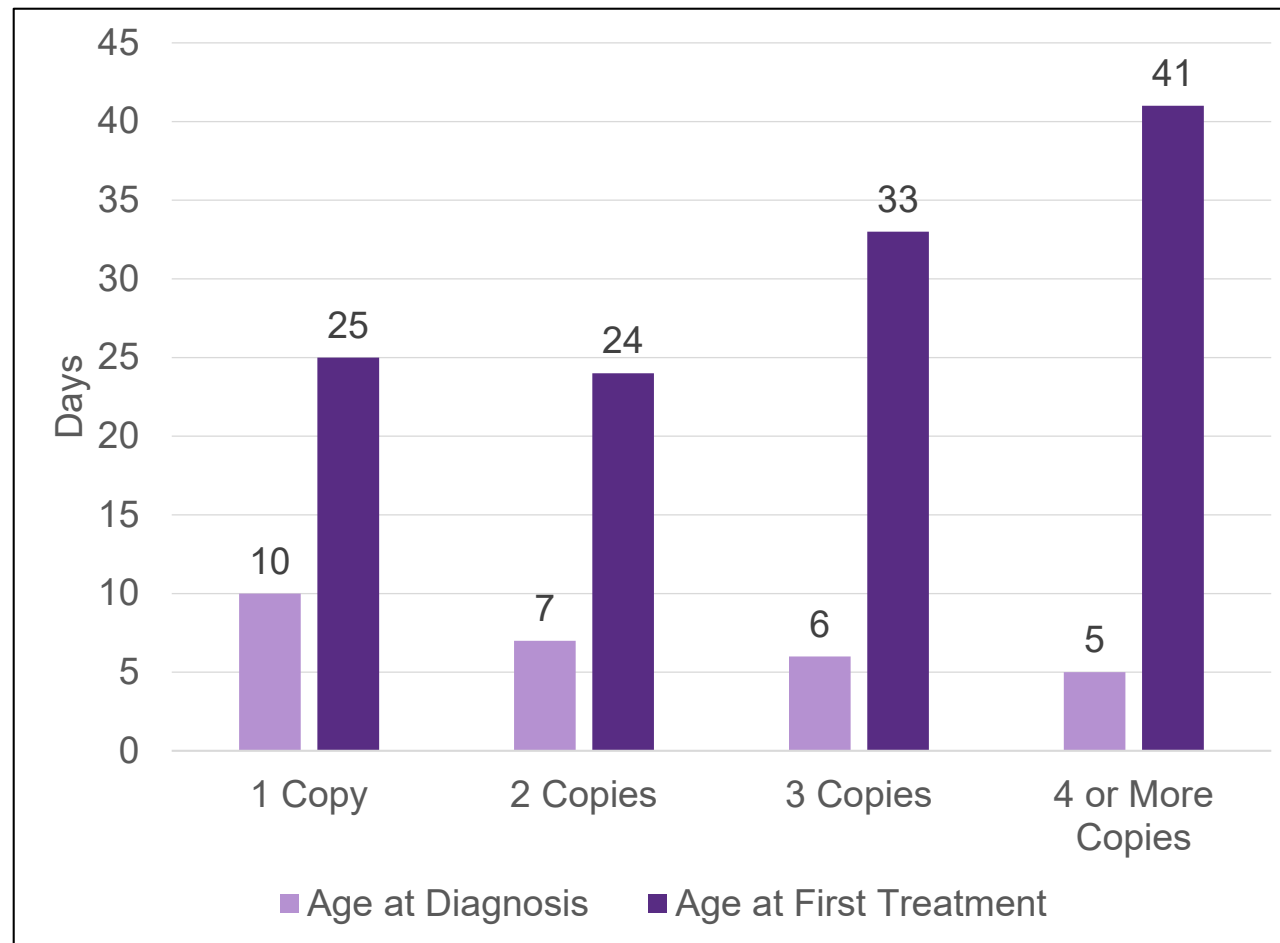


Table 1. Summary Statistics of Age (in days) to Diagnosis for All Newborns

Age at Diagnosis	
Number of Newborns	28
Mean	8
SD	5
Median	6
Range	0-22

Table 2. Summary Statistics of Age (in days) of First Treatment by SMN2 Copy Number

	1 Copy	2 Copies	3 Copies	4 or More Copies
Number of Newborns	3	11	6	4
Mean	57	39	45	148
SD	59	32	31	226
Median	25	24	33	41
Range	20-126	9-123	14-102	23-487

Future Plans

- Evaluate SMA NBS outcomes across the Cure SMA Real World Evidence data sources and others
 - Time to diagnosis
 - Time to treatment
 - Symptom spectrum
 - SMA phenotype

THANK YOU!

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